Remarks

Claims 1-37 are pending in the subject application. By this Amendment, Applicants have canceled claims 3-8 and 12-37, amended claims 1, 9, and 11, and added new claims 38-42. Support for the amendments and new claims can be found throughout the subject specification and in the claims as originally filed (see, for example, previously pending claim 37, page 12, line 24 through page 13, line 9 and page 28, lines 24-25). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1, 2, 9-11 and 38-42 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Claims 1, 2, 9, 10 and 37 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Office Action argues that Applicants have shown the formation of particular co-crystals, such as those recited within claim 11, but do not exemplify the formation of all co-crystals containing any solid API and any-co-crystal former that is liquid or solid and where the components are hydrogen bonded to one another or co-crystals with any of the numerous and diverse different co-crystal formers recited in claim 2 or the APIs recited within claim 6. The Office Action also indicates that the specification describes only the preparation of the particular co-crystals recited within claim 11 and does not describe the claimed invention in a manner sufficient to convey that the inventors were in possession of the entire claimed invention, including the formation of co-crystals containing any API and any co-crystal former that are hydrogen bonded. Applicants traverse.

It is incumbent upon the Patent Office to clearly establish that the as-filed specification fails to provide an adequate written description for the claimed invention. As set forth at § 2163(III):

> A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See, e.g., *In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971). The examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *Wertheim*, 541 F.2d at 263, 191 U.S.P.Q. at 97. In rejecting a claim, the examiner must set forth express findings of fact regarding the above analysis which support the lack of written description conclusion. These findings should:

(A) Identify the claim limitation at issue; and

(B) Establish a *prima facie* case by providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed. A general allegation of "unpredictability in the art" is not a sufficient reason to support a rejection for lack of adequate written description.

In the case of the instant application, Applicants respectfully submit that a *prima facie* case providing reasons why one skilled in the art would not have recognized that the inventor was in possession of the claimed invention has not been established. Rather, the Office Action makes a general allegation that the as-filed specification fails to provide adequate written description of the claimed invention because the examples do not exemplify or otherwise show the formation of all co-crystals.

Applicants also respectfully submit that compliance with the written description requirement does not turn on the number of examples provided in the as-filed specification. Specifically, the Federal Circuit held that "and in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure" (see *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 U.S.P.Q.2d 1001 (Fed. Cir. 2006). Accordingly, Applicants respectfully request that the rejection be withdrawn as it fails to establish a *prima facie* case that the written description provided by the as-filed specification is insufficient.

Claims 1, 2, 9, 10 and 37 are rejected under 35 U.S.C. §112, first paragraph, as nonenabled by the subject specification. The Office Action argues that the undue experimentation would be required to practice the claimed invention because the formation of different crystalline forms of APIs is unpredictable due to the numerous factors that must be controlled in order to provide different crystal states as well as the unpredictability in predicting the different types of crystals that may exist. The Office Action also argues that the specification fails to teach adequate process parameters for making the claimed co-crystals and that the as-filed specification fails to provide adequate guidance in this regard as well. Finally, the Office Action argues that undue

experimentation would be required in order for one skilled in the art to fully make and use the claimed invention. Applicants traverse.

Applicants respectfully submit that the as-filed specification clearly enables the claimed invention. For example, the as-filed specification sets forth those substances that are co-crystal formers as well as APIs (see Tables I-IV). These tables also set forth various functional groups found on the disclosed APIs and co-crystal formers as well as those moieties that interact with the disclosed functional groups (see also page 12, line 24 through page 32, line 20. Thus, the as-filed specification clearly provides teachings to those skilled in the art as to the starting materials suitable for use in the claimed invention.

The as-filed specification also sets forth at least one high throughput method for the preparation of co-crystals (see pages 43-44, referring to the CRYSTALMAX platform). The use of the CRYSTALMAX platform is described in U.S. Patent Application Publication 2002/0177167 A1 and 2002/0048610 A1. Additional high throughput methods for the formation of crystalline structures were also known around the time of the filing date of the instant invention (see, for example, WO 2002/52919 which discloses another high throughput method for the identification of crystalline forms of APIs).

Turning to the allegation that undue experimentation would be required to practice the claimed invention, Applicants respectfully submit that this is not the case. As noted above, the as-filed specification clearly sets forth APIs and co-crystal formers that can be used in the practice of the claimed invention. Additionally, the as-filed specification discloses at least one high throughput method for the identification of crystalline structures recited within the claims and additional high throughput methodologies for identifying new crystalline forms of APIs were known in the art at, or around the time the instant application was filed. As the Patent Office is aware, "The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed". *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (1982); *see also Ex parte Erlich* 3 U.S.P.Q.2d 1011 (B.P.A.I. 1982) (observing that although a method might be "tedious and laborious," such experimentation is

nevertheless "routine" defining "routine" experiments as those which use known methods in combination with the variables taught in the patent to achieve the expected, specific, patented result). As is clear from the foregoing discussion, the known methods exist for high throughput development of novel crystalline forms of known APIs. These methods allow one to vary a number of parameters simultaneously in order to identify new crystalline forms of known compounds. Thus, while some experimentation might be required to identify new API/co-crystal compounds and this experimentation may be "tedious and laborious", it would not be undue in view of the state of the art, the knowledge in the art and the teachings of the as-filed specification. Accordingly reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1, 2, 9-11 and 37 are rejected under 35 U.S.C. § 102(b) as anticipated by Oswald *et al.* The Office Action argues that the Oswald *et al.* publication anticipates the claimed invention as the reference teaches co-crystal forms of acetaminophen that include adducts with 4,4'-bipyridine. Applicants respectfully submit that the cited publication is not prior art to the claimed invention. The claimed acetaminophen co-crystals were disclosed in Provisional Patent Application No. 60/360,786, filed March 1, 2002 (see Example 1) and to which priority is claimed by this application. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1, 2, 9-11 and 37 are rejected under 35 U.S.C. § 102(a) as anticipated by Remenar *et al.* The Office Action argues that the Remenar *et al.* publication anticipates the claimed invention as the reference teaches co-crystal forms of itraconazole with 1,4-dicarboxylic acids (such as fumaric acid, succinic acid, and malic acid). Applicants respectfully submit that the cited publication is not prior art to the claimed invention. The claimed itraconazole co-crystals were disclosed in U.S. Patent Application 10/449,307, filed May 30, 2003 (see paragraphs 81 and 471) and to which priority is claimed by this application. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1, 2, 9-11 and 37 are rejected under 35 U.S.C. § 102(a) as anticipated by Fleischman *et al.* The Office Action argues that the Fleischman *et al.* publication anticipates the claimed invention as the reference teaches co-crystal forms of carbamazepine with benzoquinone, saccharin, nicotinomide, trimesic acid, 5-nitroisophthalic acid and adamantine-1,3,4,5-tetracarboxylic acid. Applicants respectfully submit that the cited publication is not prior art to the claimed invention.

The claimed carbamazepine co-crystals were disclosed in U.S. Patent Application 10/378,956, filed March 3, 2003 (see paragraph 39) and to which priority is claimed by this application. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1, 2, 9-11 and 37 are rejected under 35 U.S.C. § 102(a) as anticipated by Dvorkin *et al.* Claims 1-2, 9-10, and 37 are rejected under 35 U.S.C. § 102(e) as anticipated by Almarsson *et al.* (U.S. Patent No. 6,559,293). Claims 1, 2, and 10 are rejected under 35 U.S.C. § 102(e) as anticipated by Childs (U.S. Patent Application Publication No. 2004/0176335, published September 9, 2004). The Office Action argues that the Dvorkin *et al.* reference anticipates the claimed invention as it teaches co-crystals of hydrochlorothiazide and that the Almarsson *et al.* patent anticipates the claimed invention on the basis it teaches co-crystals of topiramate and caffeine. The Office Action argues that the Childs publication anticipates the claimed invention on the basis that it teaches co-crystals of fluoxetine HCl and succinic acid. Applicants respectfully submit that these rejections are moot in view of the amendments made to the claims cancelling the recited topiramate, hydrochlorothiazide, and fluoxetine co-crystals. Support for the exclusionary language presented in claim 1 can be found in previously pending claim 34 (now incorporated into independent claim 1) and the as-filed specification (at page 28, lines 24-25 ) where it is indicated that that any API listed in Table IV can be excluded from the invention (*e.g.*, hydrochlorothiazide). Accordingly, reconsideration and withdrawal of each rejection is respectfully requested.

Claims 1, 2, 9-11 and 37 are rejected under 35 U.S.C. § 102(e) as anticipated by Zaworotko *et al.* (WO 03/074474). The Office Action argues that the Zaworotko *et al.* publication anticipates the claimed invention as the reference teaches various co-crystals encompassed by the rejected claims. Applicants respectfully submit that the cited publication is not prior art to the claimed invention. The claimed co-crystals were disclosed in Provisional Patent Application No. 60/360,786, filed March 1, 2002 (see, for example, pages 5-6 and Examples 1-5 at pages 11-15) and to which the benefit of priority is claimed by this application. The earliest claimed filing date of the cited reference is also March 1, 2002 via the same priority document. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Claims 1, 2, 9-11, and 37 are rejected for "obviousness type" double patenting over claims 1-10 of U.S. Patent No. 7,078,526 (Remenar *et al.*). Claims 1, 2, and 10 are provisionally rejected on

the ground of nonstatutory "obviousness-type" double patenting over claims 86-93 of copending Application No. 10/546,963. Claims 1, 2, 9-11, and 37 are provisionally rejected on the ground of nonstatutory "obviousness-type" double patenting over claims 1-49 and 72-87 of copending Application No. 10/570,405 (U.S. Patent Application Publication No. 2007/0021510 to Hickey *et al.*), over claims 66-72 of copending Application No. 10/551,014 (U.S. Patent Application Publication No. 2006/0223794 to Bourghol Hickey *et al.*), and over claims 2-7, 16, and 18 of copending Application No. 10/926,842 (U.S. Patent Application Publication No. 2005/0070551 to Remenar *et al.*). Applicants respectfully request that these rejections be held in abeyance until such time that allowable subject matter is indicated.

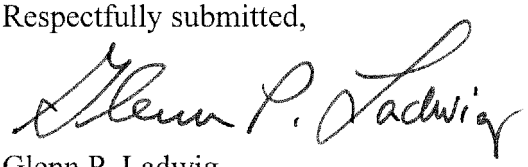
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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